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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,852	08/04/2003	Jean-Yves Marcel Paul Bonnefoy	1430-284	5060

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,852	BONNEFOY, JEAN-YVES MARCEL PAUL	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/817,719.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/4/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a continuation of USSN 08/817,719, which is the national stage entry of PCT/EP95/04109.

Claims 1-8 are pending in this application

Applicant's election of the species of rheumatoid arthritis in the reply filed on September 19, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The art search has been extended beyond the elected species.

Claims 1-8 are under examination in the instant application.

Information Disclosure Statement

2. Applicant's IDS received August 4, 2003 is acknowledged and has been considered.

Specification

3. Applicant's amendment to the specification received August 4, 2003 is acknowledged. Applicant is reminded to update the first line of the specification to indicate that USSN 08/817,719 is now US Patent No. 6,627,195.

Claim Objections

4. Claim 1 is objected to because it appears that a typographical error has occurred and that the currently recited "administrating" in line 2 of claim 1 should be changed to "administering".

Claim 4 is objected to because the accepted notation for the claimed antibody fragment is "$F(ab')_2$", not "$F'(ab')_2$" as is currently recited in the claim.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of administering an antibody that binds CD23 and blocks the interaction of CD23 and CD11b or that blocks the interaction of CD23 and CD11c for the treatment of an inflammatory disease, does not reasonably provide enablement for administering any binding agent that blocks the interaction between CD23 and CD11b or CD11c to treat any inflammatory disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has claimed a method of administering a binding agent to treat an inflammatory disease. The identity of the target molecule bound by the binding agent is

not recited, but the claims do indicate that said binding agent blocks the interaction between CD23 and CD11b or CD11c. The specification provides working examples wherein an antibody that specifically binds CD23 is effective in reducing symptoms in mouse collagen induced arthritis, an art recognized model system that resembles rheumatoid arthritis (see particularly examples 1-4). The specification does not appear to define the scope of the term "binding agent", but it appears reasonable that the binding agent, in addition to being an antibody or fragment of an antibody that binds CD23, could also be antibodies or fragments that bind CD11b or CD11c, and soluble CD23 (sCD23). This is because antibodies that bind CD11b or CD11c would effectively block interaction with CD23, and sCD23 would bind to CD11b and CD11c in the same manner as CD23, thus effectively competing with CD23 for binding to CD11b and CD11c. Note that CD23, CD11b, and CD11c are membrane bound proteins that are expressed on the plasma membrane of cells. Given that CD23 is also known as FcεRII, molecules of IgE could also potentially serve as "binding agents" since they would bind CD23 and block it from interacting with other molecules. Other possibilities for the recited binding agent are agents that decrease the surface expression of CD23, CD11b, or CD11c, examples of such agents being DNA binding proteins including transcription factors and other proteins that modulate the expression level of cellular polypeptides. Transcription factors and other protein expression modulating agents do not appear to be discussed in the instant specification.

The claims indicate that administration of the "binding agent" (whatever its structure and binding specificity may be) results in the treatment or prophylaxis of an

inflammatory disease. As discussed above, numerous binding agents can potentially be used in the instant claimed methods, and these include antibodies that bind CD11b and CD11c. Lecoanet-Henchoz et al. teach that administration of whole antibody that binds CD11b and Cd11c induces the release of the inflammatory molecules IL-1b, IL-6, and TNFα, while administration of Fab fragments of the same antibodies do not cause a similar release of cytokines, yet both block the interaction with CD23 (of record as reference XR on the IDS received 8/4/03, see entire document, particularly the abstract and Figures 2, 5 and 6). Whole antibody and monovalent Fab fragments that bind CD11b or CD11c are all "binding agents" within the scope of the claims, but administering whole antibody exacerbates, rather that treats, an inflammatory disease due to the release of additional inflammatory cytokines. Similarly, Armant et al. teach that administration of sCD23 triggers the release of the inflammatory cytokine TNFα, and that sCD23 is itself a proinflammatory cytokine (of record as reference ER on the IDS received 8/4/03, see entire document, particularly the abstract and Figures 5 and 6). Rezzonico et al. teach that administration of antibodies to CD11b and CD11c, as well as administration of sCD23, leads to the release of macrophage inflammatory proteins (MIP)-1α, MIP-1β, and IL-8 (Blood, 2001, 97:2932-2940, see entire document, particularly the abstract, the first full paragraph of the right column of page 2934, the paragraph spanning the left and right column of page 2935, and Figure 3). As such, administering molecules encompassed by the scope of "binding agent" recited in the claims often leads to a worsening of the inflammatory disease that is being treated due to the release of additional inflammatory cytokines.

The instant claimed methods also recite that administration to a human of such "binding agents" can be used in the prophylaxis of an inflammatory disease. Stedman's Medical Dictionary, 27th edition, defines prophylaxis as prevention of a disease or of a process that can lead to a disease (see provided definition downloaded 11/7/05). As such, prophylaxis of an inflammatory disease requires that administration of the "binding agent" occur prior to the start of the inflammatory disease such that it can be prevented. Many inflammatory diseases, rheumatoid arthritis included, are only clinically diagnosed upon presentation with the characteristic signs and symptoms of the disease (The Merck Manual, 17th edition, 1999, pages 416-423, see entire document, particularly the subsections Symptoms and Signs beginning on page 416 and Diagnosis beginning on page 417). Therefore, to practice the full scope of the claimed invention, a clinician would need to initiate administration of the "binding agent" prior to diagnosing a patient with an inflammatory condition. Further, it is not clear that blocking the interaction of CD23 with its potential ligands, or conversely, blocking the interaction of CD11b or CD11c with their potential ligands, will effectively treat any and all inflammatory diseases. The causes of many inflammatory diseases are unknown, and as such it cannot be predicted with certainty which patients will and which patients will not develop an inflammatory disease such as rheumatoid arthritis given the current state of medical knowledge (Merck Manual, see particularly the subsection Etiology and Pathology).

Therefore, based upon the breadth of the term "binding agent", the apparent lack of working examples demonstrating administration of binding agents other that anti-CD23 antibodies, the teachings of the art concerning how administration of molecules

that are reasonably encompassed by the term "binding agents" induces the release of inflammatory cytokines and would therefore exacerbate rather than treat an inflammatory disease, and the requirement that the method be performed on a patient prior to the patient being diagnosed with an inflammatory disease in order to achieve prophylaxis of the disease, and the lack of evidence that blocking the interaction of CD23 with its ligands or of blocking the interaction of CD11b or CD11c with their ligands will effectively treat all inflammatory diseases especially since the causes of many inflammatory diseases are not known, a skilled artisan would be unable to make and use the full breadth of the claimed invention without conducting additional research.

7. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The breadth of applicant's claims read on the administration of any "binding agent" to treat an inflammatory disease, the only limitation placed upon the "binding agent" being that it blocks the interaction of CD23 with CD11b or CD11c. No structure that gives rise to this functional property of blocking the interaction between CD23 and either CD11b or CD11c is recited in the base claim, and while dependent claims recite that the "binding agent" is an antibody, the antigen to which the antibody binds is not recited. The specification does not provide a definition of "binding agent" that clearly

delineates it scope, but the specification does specifically teach the administration of an anti-CD23 antibody as an agent that treats an inflammatory disease (see particularly examples 1-4), and as such applicant is clearly in possession of anti-CD23 antibodies as "binding agents". The specification does not appear to teach any particular structure that must be present in a "binding agent" such that it has the functional ability to block the interaction between CD23 and CD11b or CD11c nor does it appear to teach which molecule or molecules are being specifically bound by said "binding agent". Therefore, applicant is not in possession of the entire genus of molecules encompassed by the term "binding agent".

Molecules that are known to specifically bind CD23 include whole IgE, peptides derived from the Fc domain of IgE, CD21, CD11b, CD11c and anti-CD23 antibodies (Bonnefoy et al., Int Rev Immunol, 1997, 16:113-128, see entire document particularly the abstract). The breadth of "binding agents" is not limited to these agents since the target that is specifically bound by the "binding agent" is not recited. As such, agents that bind CD11b or CD11c are also encompassed by the instant claims and include CD11b and CD11c themselves (since CD23 cannot simultaneously bind both molecules), antibodies that specifically bind CD11b or CD11c, and other agents known to bind these molecules including C3b, LPS, zymosan, ICAM-1, and ICAM-2 (Ehlers, MR, Microbes and Infection, 2000, 2:289-294, see entire document, particularly section 4, Molecular promiscuity, beginning in the right column of page 290). The breath of the claims also read on small molecule pharmacological inhibitors of the interaction of CD23 with CD11b or CD11c, and can even be extended to the use of agents that specifically

bind ribosomes and disrupt protein synthesis or that bind DNA and alter the transcriptional activity of the cell since the claims encompass the use of any agent, as long as the agent specifically binds something. Note that the use transcription and translation inhibitors would result in CD23, CD11b, and CD11c not being expressed on the surface of the cell, and if the molecules are not surface expressed they cannot interact, thus effectively blocking their interaction.

The specification does not appear to define a core structure that must be maintained by all "binding agents" that mediates the functional activity of blocking the interaction of CD23 with CD11b or CD11c, and given the breadth of what is reasonably included as a "binding agent" and their diverse structures and mechanisms of operation, it is not clear that such a structure could be readily described. As such, applicant has failed to adequately disclose what would be required for a molecule to be recognized by a skilled artisan as "binding agent" since the structure required of a "binding agent" does not appear to be disclosed other than in the specific example of anti-CD23 antibodies. Thus, Applicant was not in possession of the claimed genus of methods that utilize all "binding agents". Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 5, and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Lynch et al. (US Patent No. 5,766,943, see entire document).

Lynch et al. teach that IgE is responsible for the pathology of allergy and that administration of human soluble CD23 (sCD23) is to be used to treat human patients suffering from allergic responses mediated by IgE (see entire document, particularly lines 47-53 of column 2 and lines 5-53 of column 18). A specific disease taught by Lynch et al. as amenable to such treatment is asthma (see particularly lines 9-11 of column 18). It is noted that Lynch et al., do not teach that sCD23 inhibits the binding of CD23 with CD11b or CD11c. However, given that the domain of sCD23 that binds to CD11b or CD11c is the same domain found in CD23 (a membrane-bound cell surface expressed molecule) that mediates the interaction of CD23 with CD11b or CD11c, it is inherent that sCD23 would compete for binding with CD23 for binding to CD11b or CD11c *in vivo*. As such, sCD23 is a "binding agent" consistent with the limitations disclosed for such a molecule in the specification and claims, and therefore the methods of administration taught by Lynch et al. anticipate the instant claimed methods.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,627,195. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims recite a method for treating an inflammatory disease by administering an agent that binds CD23 and therefore anticipate the instant claims. This is because the scope of the instant methods encompasses the administration of any binding agent of any specificity so long as it blocks the interaction of CD23 with CD11b or CD11c, and an agent that binds specifically to CD23 is part the genus of "binding agents" recited in the instant claims.

12. Claims 1-3 and 5-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 23 of copending

Application No. 09/674,716. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 23 is drawn to administering a monoclonal antibody that binds CD23 for the treatment of rheumatoid arthritis, and as such it anticipates the instant claims because the anti-CD23 antibody is a "binding agent" and rheumatoid arthritis is an inflammatory disease.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 8, 2005

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